Problem Set 3
Due 3 May 2000

140.668 Statistical Genetics

1. Calculate the IBD distribution (at the disease gene) for a *discordant* sib pair (one affected, one not affected) in the case of a single, fully penetrant, recessive disease gene (i.e., penetrances $f_0 = f_1 = 0$, $f_2 = 1$), when the disease allele frequency is $p = 0.05$, assuming random mating and Hardy-Weinberg equilibrium.

2. Calculate the IBD distribution for the pair as in (1) at a marker which is a recombination fraction 5% away from the disease gene.

3. Consider a set of four affected siblings. Calculate the values of S_{pairs} and S_{all} when their inheritance vector is (a) [(1,3),(1,3),(2,4),(2,4)] and (b) [(1,3),(1,3),(1,4),(1,4)].

4. Consider a set of three affected siblings. Let S_{ij} = number alleles that siblings i and j share IBD at a particular position, and let $S_{\text{pairs}} = (S_{12} + S_{13} + S_{23})/3$. (a) Show that, under the null hypothesis of no linkage, $\mathrm{E}(S_{ij}) = 1$, $\mathrm{var}(S_{ij}) = 1/2$, and $\mathrm{cov}(S_{ij}, S_{ij'}) = 0$. (b) Use these results to calculate the mean and variance of S_{pairs} under the null hypothesis.

5. Consider a quantitative trait which is under the control of a single diallelic gene with alleles A and B, so that individuals with genotype AA, AB, and BB, have mean trait value $\mu - a$, $\mu + d$ and $\mu + a$, respectively. Consider a randomly ascertained sibpair with trait values X_1 and X_2. Assume random mating, Hardy-Weinberg equilibrium, and no shared environment effect. Calculate $\mathrm{var}[(X_1 - X_2)^2|$ sibs share k alleles IBD].